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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/609,346	06/26/2003	Zailin Yu	ZYU-0603	1103

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/609,346	YU ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-50 have been canceled. New claims 51-67 (11/21/2006) are under consideration by the Examiner.

2. Receipt of applicant's arguments filed on 11/21/2006 is acknowledged.

3. The following previous objections and rejections are withdrawn in light of applicants amendments filed on 11/21/2006:

(i) the rejection of claims 21-23, 27-33, 40-41 under 35 USC 112, first paragraph for lack of adequate written description;

(ii) the rejection of claims 21-23, 27-33, 40-41 under 35 USC 112, first paragraph for scope of enablement; and

(iii) the rejection of claims 21-23, 27-31, 33, 40-41 under 35 USC 112, second paragraph.

Applicant's arguments with respect to claims 21-23, 27-31, 33, 40-41 have been considered but are moot in view of the new ground(s) of rejection over claims 51-67.

4. Applicant's arguments filed on 11/21/2006 have been fully considered and were persuasive in part. The issues remaining as well as new issues are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. The use of the trademark ATCC has been noted in this application. It should be capitalized whenever it appears and be accompanied by the ® symbol.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim rejections-35 USC § 112, first paragraph

7. Claim 51 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. When biological material is required to practice an invention, and if it is not so obtainable or available, the enablement requirements of 35 USC §112, first paragraph, may be satisfied by a deposit of the material. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining ATCC Deposit No. PTA-4607 and it does not appear to be a readily available material. The ATCC® PTA-4607 deposit in full compliance with 37 CFR §§ 1.803-1.809 would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claim rejections-35 USC § 112, second paragraph

8. Claims 51-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 51, 61-67, are vague and indefinite because they recite "constructed polynucleotide" rather than the conventional "recombinant polynucleotide....".

Claim 52 is vague and indefinite because it recites "claims 51" rather than "claim 51".

Claim 53 recites the limitation "the sequence" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 63 recites the limitation "the constructed isolated polynucleotide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 54-60 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 103

9. Claims 51-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw (4,904,584) in view of the Capon et al. patent (U.S. Patent No. 5,116,964).

This rejection is maintained for reasons of record set forth at pages 7-8 of the previous Office action (8/24/2006).

Applicants have traversed this rejection on the grounds that "to establish a *prima facie* case of obviousness, there must be some motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine reference teachings (MPEP at 2143)". However, the motivation to combine the references as well as a reasonable expectation of success has been provided in the Capon reference (column 5, lines 11-21).

Applicants argue that the prior art does not teach or suggest the subject matter claimed in claim 51. However, contrary to Applicants arguments, if the prior art explicitly taught this limitation being claimed the instant rejection would be a 35 USC 102(b) rejection rather than a 35 USC 103 rejection. Pertinent to the instant case, is the motivation for modification of G-CSF, which has been provided by the reference by Capon et al. This rejection is a classic 35 U.S.C.

§ 103 rejection with a primary reference teaching chimeric proteins for directing ligand binding partners such as growth factors, hormones or effector molecules to cells bearing ligands for the ligand binding partners comprising a ligand binding partner fused to a stable plasma protein which is capable of extending the in vivo half-life of the ligand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is a human serum albumin protein (HSA) i.e. providing the motivation to add the HSA to a ligand and a secondary reference teaching the nucleotide and corresponding amino acid sequence of G-CSF and site-specific homogenous modification of G-CSF having amine reactive groups that are suitable for modification. The Examiner does not disagree with Applicants that Shaw does not teach both G-CSF and HSA. As stated earlier, Shaw has only been relied upon for the disclosure of the method of producing recombinant G-CSF using the DNA encoding G-CSF. This observation was known in the art at the time of filing of the instant invention by Applicants, and furthermore, Applicants have not shown evidence or arguments to prove otherwise.

The Capon patent is being relied upon to demonstrate that it was well known in the art at the time of the invention that production of a chimeric protein containing the albumin fused to any soluble protein would increase the circulating half-life of the protein. Applicants respond that the scope of the '964 patent is immense (see column 7, lines 19-34). Applicants are absolutely correct, the teaching of Capon could be taken by any skilled artisan to encompass "any" soluble protein. The Capon teaching is a general teaching detailed in column 5, lines 11-20, that:

"The objects of this invention are accomplished by providing novel polypeptides comprising a ligand binding partner fused to a stable plasma protein which is capable of

extending the in vivo half-life of the ligand binding partner when present as a fusion with the ligand binding partner, in particular wherein such a stable plasma protein is an immunoglobulin constant domain."

Applicants again argue that Shaw does not provide motivation to modify G-CSF in any way and that the '964 patent, despite its very broad general disclosure, does not suggest modifying G-CSF, and therefore this combination of references cannot render obvious the specific HSA/G-CSF chimera recited in the present claims. However, contrary to Applicants arguments, it is Capon that provides the express motivation to add the albumin to any soluble protein to increase its circulating half-life. A cytokine such as G-CSF, is a soluble protein which is a growth factor which acts on a specific population of cells i.e. the cells of the hematopoietic system.

Applicants also point out that specific proteins are disclosed by the '964 patent but CSF-1 is excluded. It is pointed out that if the Capon et al patent disclosed the instant HSA/G-CSF fusion claimed, the instant rejection would be a 35 U.S.C. § 102(b) rejection, rather than a 35 U.S.C. § 103 rejection.

Applicants argue that the disclosure of a genus of fusion proteins in Capon fails to render species within the genus *prima facie* obvious. However, contrary to Applicants arguments, any species within a genus is obvious unless the species has properties unexpected in the genus. In the instant case, there is no unexpected property in the species product being claimed because the fusion would have been expected to have the increased half-life as taught by Capon.

Applicants arguments that the fusion protein art in general is unpredictable, is also unpersuasive because the vast majority of generic proteins in Class 435, are predicated on the

presumption that one can reasonably fuse a first protein to a second protein and expect success. An example of fusion proteins that lose their activity are "secropins" and other proteins in which a free amino or carboxy group are absolutely essential for activity. The vast majority of proteins do not require a free amino or carboxy group for activity. A 35 U.S.C. 103 rejection is based on reasonable expectation of success, not absolute certainty. To reason that the vast majority of the embodiments of the Capon et al patent are non-functional, are without foundation, because the claims in the Capon patent are valid and a vast majority of the embodiments would retain functionality. Applicants allege surprising results that Applicants obtained prolonged protection with G-CSF, however, the results, contrary to being surprising, would be what the prior art predicted.

Conclusion

No claim is allowed.

Claims 51-67 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
December 5, 2006